LECTURE 1

RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

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OBJECTIVES

- To understand basis of rheumatic fever as an immunologically mediated late complication of **Streptococcal infection**
- To know that autoimmunity results from production of **cross reacting antibodies against Streptococcal antigens**
- To describe rheumatic heart disease as one of the several **manifestations of rheumatic fever**
- To know the **signs, symptoms, pathogenesis, treatment and prophylaxis** of rheumatic heart disease

RHEUMATIC FEVER

Epidemiology

- **3%** of people with untreated **group A streptococcal pharyngitis** develop rheumatic fever.
- **15-20 million** new cases a year in developing countries.

Definition

It is an **inflammatory** disease which may develop after a **Group A Streptococcal** infection

E.g. ***Strep. throat infection, Scarlet fever.***

- Can involves the **heart, joints, skin, and brain**
- Most common in ages **5-15**
- Antigen-presenting cells bearing the **HLA-DR7** molecule from RHD patients recognize **heart-tissue protein.**

Organism

Group A streptococcus

Latent period: 1-5 weeks

- Group A b-haemolytic streptococcus
  - All cases with infection

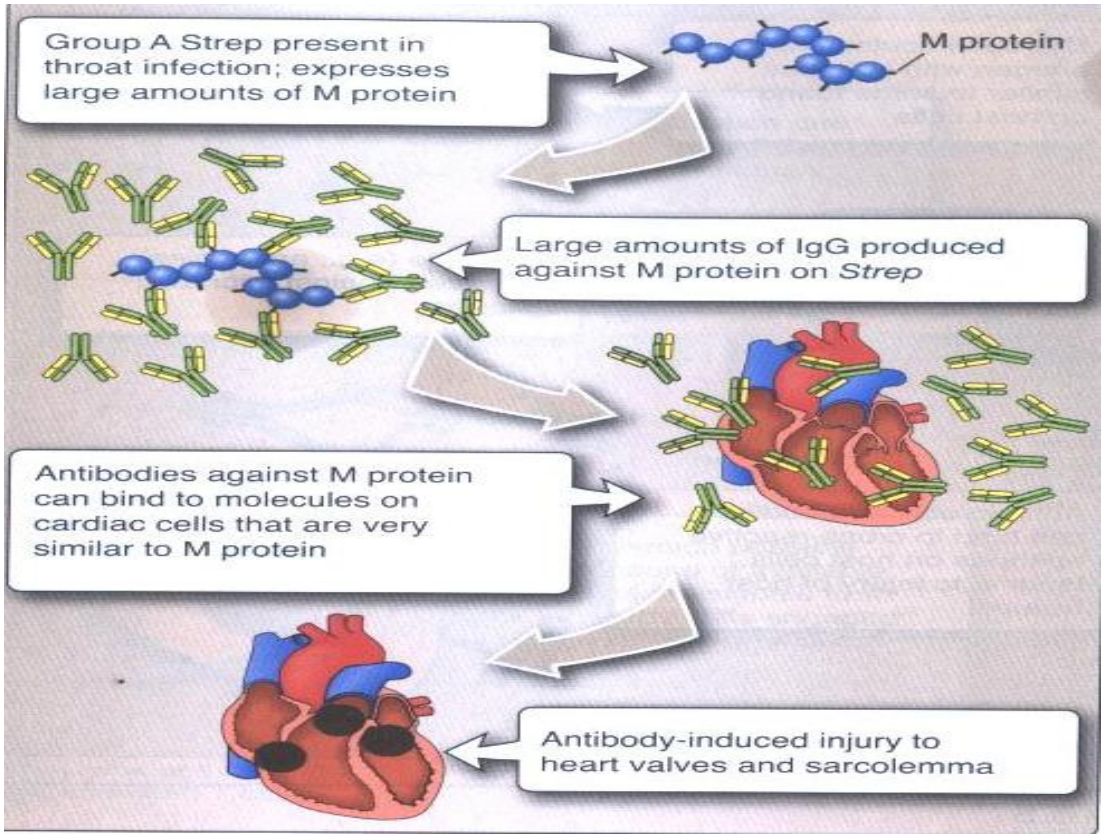
    E.g. *Pharyngitis*
- Post streptococcal ***glomerulonephritis*** is caused by **antigen-antibody** complexes **(Type III hypersensitivity)**

Virulence Factors

M proteins	Attachment & interferes with host immune response
Hyaluronic acid capsule	Camouflages the bacterium
Streptokinase	Dissolves blood clots
Peptidases	Degrades proteins involved in immune response
Pyrogenic toxins	Stimulate fever, rash & shock
Streptolysins	Lyse erythrocytes, leukocytes & platelets

Pathogenesis

- Rheumatic fever affect the **peri-arteriolar** connective tissue.
- Believed to be caused by **antibody cross-reactivity.**
- **Type II** hypersensitivity (molecular mimicry)
- Activation of the endothelium means it express **vascular cell adhesion molecule-1 (VCAM-1)** which will attract T cells to penetrate the valve and cause inflammation.



Group A streptococci cell wall contains ‘M protein’ (highly antigenic)

Immune system generates antibodies against ‘M protein’ which cross react with **cardiac myofiber protein myosin and smooth muscle cells of arteries**

Which induces **cytokine release** and tissue destruction

Inflammation occurs through direct attachment of complement and Fc receptor-mediated recruitment of **neutrophils and macrophages**

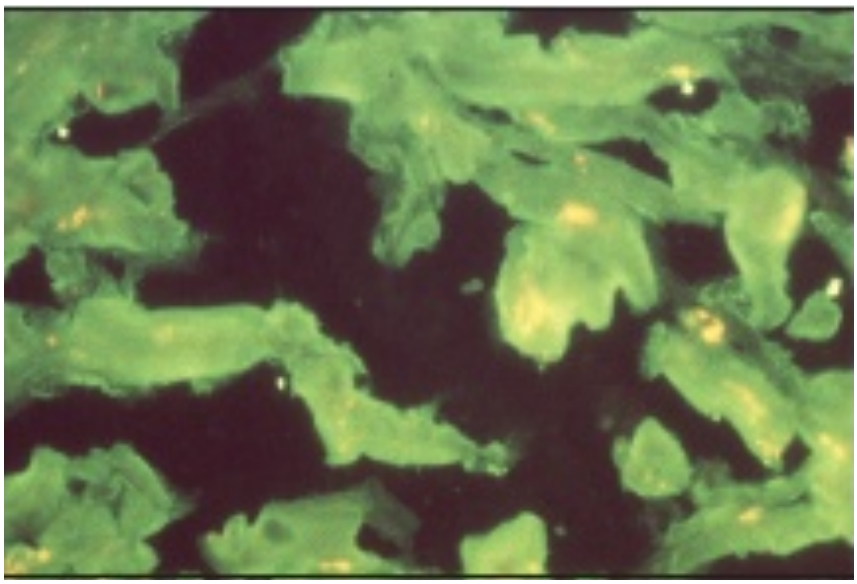
Pathophysiology

- **During a Strep. Infection**

Activated antigen presenting cells such present the bacterial antigen to helper T cells.

Helper T cells then activate self reactive B cells & induce the production of antibodies against the cell wall of Streptococcus

- The antibodies may also react **against the myocardium and joints > rheumatic fever.**



Immunofluorescent staining of heart muscle with serum to diagnose.

Clinical Presentations

Heart	• 60% of ARF progress to RHF • **Pancarditis** • Valvular damage (mital valve is most common)
Joints	• **Polyarthritis**: flitting from joint to joint (migratory), affecting the larger joints. • Swelling, redness, tenderness and joint effusions
Skin	• Skin lesions • **erythema marginatum**—large erythematous lesions with prominent margins slightly raised
CNS	• **Sydenham's chorea** • The choreiform movements affect the head & upper limbs • May be generalized or restricted to one side of the body (hemi-chorea) • Chorea eventually resolves completely, within 6 weeks.
Subcutaneous	• **Subcutaneous nodules:** painless, round, firm lumps overlaid by normal looking skin. • Range from a few millimeters to 1.5 cm in diameter, localized over bony prominences like the elbow, shin and spine. • Sometimes last longer than a month.

Investigations

- **Anti-streptolysin O (ASO) titer**
  - 80% of patients with ARF have an elevated anti-streptolysin O titer at presentation
  - Rising titer is more convincing
- **Anti-DNAse B test**
- **Anti-hyaluronidase test**
- **Throat culture for group A streptococci**
  - (obtain 2 or 3 cultures)

Treatment

- Treat first strep throat infection with **penicillin**
- Treat other manifestations **symptomatically**
- **Prophylactic** long term **anti-strep therapy** given to anyone who has had rheumatic fever.

Clinical Course

Subsequent attacks (recurring)

Increased vulnerability to reactivation of disease with subsequent strep infections

- **Same symptoms** with each attack
- **Carditis** worsens with each attack
- **Heart valves** are frequently deformed (mitral)
- **Hear failure** develops after decades

Acute, Recurring, Chronic:

- **Symptoms prone to recur with subsequent Strep. infections**
- **Chronic disease leads to fibrosis**

(chordae of heart valves + valve cusps)

REMEMBER

- Rheumatic heart disease results from **cross reacting antibodies** binding the heart valves
- **Repeated attacks** of Streptococcal throat infection over the years **damage heart valves** resulting in either stenotic or incompetent heart valves
- Treatment involves **surgical replacement** of the damaged heart valves
- In patients with rheumatic fever **long term administration of penicillin** is recommended for prevention of future infections by group A Streptococcus

MCQS

1- Which of the following valves is most affected in RHD?

A- Pulmonary B- Aortic C- Mitral

2- What is a CNS presentation in ARF?

A- Sydenham's chorea B- erythema marginatum C- Polyarthritis

3- Which of the following dissolves blood clots?

A- Peptidases B- Streptokinase C- Streptolysins

1 C, 2 A, 3 B